## REMARKS

Courtesies extended to Applicants' representative in the personal interview held on July 30, 2008, are acknowledged with appreciation. The content of the interview is substantially as set forth in the Examiner Interview Summary, and the comments which follow.

No claim amendments are presented at this time. Accordingly, claims 1-26 and 28-33 remain pending. The present status of all claims in the application is provided in the Listing of Claims presented herein beginning on page 2 of this communication.

**Rejection under 35 U.S.C. § 112, first paragraph**

The withdrawal of the rejection of claims 23-25 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement, is acknowledged with appreciation.

**Rejection under 35 U.S.C. § 112, second paragraph**

The rejection of claim 9 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite, is respectfully traversed. Applicants respectfully disagree with the Examiner's assertion that the phrase "adapted to provide a pharmacologically effective amount of granisetron after about 2 hours" is allegedly unclear (see page 2, lines 11-12 of the Office Action). Contrary to the Examiner's assertion, the language at issue is submitted to be clear. One of skill in the art would readily understand the above-quoted language to indicate that the patch can deliver amounts of the active ingredient, granisetron, capable of doing that which granisetron is known to do, e.g., prevent nausea and vomiting in a subject undergoing chemotherapy, within 2 hours of being administered to the patient; i.e., invention patches can be administered to a patient, and within 2 hours, chemotherapy can start. Consistent with this discussion, the Examiner's attention is directed to paragraph **[0035]** of Applicants' specification, which indicates that "the patches of the present invention can already begin to show efficacy by about 2 hours. . ."

The repeated assertions by the Examiner of alleged lack of clarity of the above-quoted claim language are submitted to be without merit. To the extent drug may be released in less than 2 hours, the amount of drug released does not reach the level required for efficacy until about 2 hours have elapsed. With respect to the phrase "pharmacologically effective amount," given the well characterized properties and benefits of granisetron, it is submitted that one of skill in the art can readily determine what is a "pharmacologically effective amount" of granisetron.

**Rejection under 35 U.S.C. § 102(b)**

The rejection of claims 1-26, 28-31 and 33 under 35 U.S.C. § 102(b) as allegedly being anticipated by Effing (WO 98/53815 A1) is once again respectfully traversed. As discussed at the personal interview, to the extent the Examiner elects to rely on the Effing reference, the reference must be considered as a whole, for all that it teaches, not just that which is convenient for the Examiner's purposes. When read as a whole, the reference teaches both the interchangeability of tropisetron and granisetron, and the undesirability of using hydroxyl-containing monomers (such as 2-hydroxyethylacrylate (HEA)) in the preparation of an adhesive patch containing tropisetron or granisetron.

As further discussed at the personal interview, Applicants' invention, as defined, for example, by claim 1, distinguishes over Effing at least by requiring an adhesive patch suitable for the transdermal administration of granisetron, wherein the adhesive is an acrylic adhesive containing non-acidic hydroxyl moieties, a physiologically effective amount of granisetron being loaded in the adhesive. Therefore, invention adhesive patches are required to contain hydroxyl moieties, but not just any hydroxyl moieties—non-acidic hydroxyl moieties.

In contrast to the present claims, which are directed specifically to adhesive patches containing granisetron, Effing is directed to adhesive patches containing either tropisetron or granisetron—suggesting that these two compounds are substantially similar both structurally and

functionally (see, for example, page 1, line 23-page 2, line 2 of Effing, which suggests the interchangeability of these compounds). Indeed, as discussed at the personal interview, virtually every reference to active drug in the Effing specification is made in the alternative:

-in the Title ("TROPISETRON OR GRANISETRON");

-in the abstract, line 5 ("selected from the group consisting of tropisetron and granisetron");

-in the abstract, line 7 ("tropisetron or granisetron");

-page 1, line 6 of the specification ("tropisetron or granisetron");

-page 1, lines 23-24 of the specification ("Tropisetron . . . and granisetron");

-page 2, line 20 of the specification ("tropisetron and granisetron");

-page 2, line 28 of the specification ("tropisetron and granisetron"); and

-page 7, line 24 ("tropisetron or granisetron").

The only exceptions throughout the Effing specification where tropisetron and granisetron are not mentioned in the same clause are found:

-in the background (at page 2, line 10) where "ondansetron and granisetron" are suggested to be interchangeable; and

-in the Examples, which deal only with tropisetron; however, based on the consistent indication throughout the Effing specification that tropisetron and granisetron are substantially interchangeable, there is no reason (absent improper reliance on Applicants' disclosure) why one of skill in the art would expect granisetron to perform any differently than tropisetron.

Moreover, not only does Effing teach the interchangeability of tropisetron and granisetron, the reference also teaches the undesirability of using hydroxyl-containing monomers (such as HEA) in the preparation of an adhesive patch containing tropisetron or granisetron. Indeed, the reference clearly teaches away from the use of any hydroxyl-containing monomer, such as HEA, in the preparation of an adhesive patch containing tropisetron or granisetron, as

evidenced by the numerous admonitions throughout the Effing specification that the B monomer should be free of nucleophilic groups (including hydroxyl):

-page 3, line 24 of the specification ("Preferably, the B monomer is free of nucleophilic groups");

-page 3, line 30 – page 4, line 1 ("Preferably, the B monomer is free of nucleophilic groups");

-page 4, lines 8-9 ("Such monomers are preferably free of groups containing nucleophilic groups as described above");

-claim 2, lines 1-2 ("said B monomers are free of nucleophilic groups");

-claim 3 lists numerous possible B monomers, but hydroxyl-containing monomers are conspicuously absent from the list of possibilities;

-claim 12, lines 1-2 ("said B monomers are free of nucleophilic groups"); and

-claim 13 lists numerous possible B monomers, but hydroxyl-containing monomers are conspicuously absent from the list of possibilities.

Thus, repeatedly throughout their disclosure, Effing asserts that "preferably, the B monomer is free of nucleophilic groups."

Indeed, the numerous admonitions throughout the Effing specification that the B monomer should be free of nucleophilic groups are fully consistent with the results of EXAMPLE 7 (at page 13 of Effing), which indicates that an adhesive prepared with 2-hydroxyethylacrylate (HEA) as monomer B suffered from a decrease in drug content of more than 10% within four weeks of storage. This stands in stark contrast to the remaining examples which evaluate the stability of the active drug in the transdermal patch. See, for example, EXAMPLE 1 and EXAMPLE 2 (both at page 11 of Effing), which indicate that full stability is retained at both 25°C and 40°C for at least four weeks with the adhesive formulations employed therein (which include no hydroxyl-containing monomers).

Furthermore, of the numerous examples of B monomers set forth at page 3, lines 11-23 of Effing, only one contains a free hydroxyl group (2-hydroxyethylacrylate, HEA). One can

question, however, why that compound is even included in the list of suitable monomers, since, as noted above, the reference, when read in its entirety, makes it clear that use of such a B monomer is disfavored.

Since all of the experiments conducted by Effing are carried out with tropisetron, Effing merely extrapolates the results with tropisetron to granisetron, based on the assertion that these two compounds are substantially similar both structurally and functionally (see, for example, page 1, line 23-page 2, line 2 of Effing, which suggests the interchangeability of these compounds). In view of Effing's teachings, one of skill in the art would expect that observations made with respect to tropisetron (the only compound with which Effing conducted experiments) would be equally applicable to granisetron. This clearly teaches against the present invention since Effing makes it clear that the only B monomer disclosed therein that contains a free hydroxyl group (2-hydroxyethylacrylate, HEA) is disfavored. Thus, one of skill in the art would have no motivation to use a hydroxyl-containing monomer such as HEA in the preparation of an adhesive patch containing tropisetron or granisetron. Even if such motivation existed, based on the teachings of Effing, one of skill in the art would have no expectation of success using tropisetron or granisetron with an adhesive such as the adhesive of Effing EXAMPLE 7. Accordingly, the results reported herein are both surprising and unexpected in view of the teachings of Effing.

It is respectfully submitted that the assertion of the Effing reference against the present claims can only be maintained by engaging in improper hindsight analysis, having benefit of Applicants' disclosure. Indeed, it is only upon engaging in improper hindsight analysis that the Examiner can advance the argument that Effing in any way suggests doing that which Applicant has done. Such use of Applicants' disclosure is clearly improper. It is, therefore, resepectfully submitted that a fair reading of Effing, when taken as a whole, actually teaches against that which only Applicants have demonstrated to be of therapeutic value, i.e., adhesive patches suitable for the transdermal administration of granisetron, wherein the adhesive is an acrylic

adhesive containing non-acidic hydroxyl moieties, with a physiologically effective amount of granisetron being loaded in the adhesive.

Thus, to the extent the Examiner elects to rely on the Effing reference, the reference must be considered as a whole, for all that it teaches, not just that which is convenient for the Examiner's purposes. When read as a whole, the reference not only teaches the interchangeability of tropisetron and granisetron, the reference also teaches the undesirability of using hydroxyl-containing monomers such as HEA in the preparation of an adhesive patch containing tropisetron or granisetron.

Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b) are respectfully requested.

**Rejection under 35 U.S.C. § 103(a)**

The rejection of claim 32 under 35 U.S.C. § 103(a), as allegedly being unpatentable over Effing in view of Sanger et al. (WO 94/01095 A2), is once again respectfully traversed. Applicants' invention, as defined by claim 32, distinguishes over the applied art by requiring a method of treatment employing the adhesive patch of claim 1, i.e., an adhesive patch suitable for the transdermal administration of granisetron, wherein the adhesive is an acrylic adhesive containing non-acidic hydroxyl moieties, a physiologically effective amount of granisetron being loaded in the adhesive. Therefore, invention adhesive patches are required to contain hydroxyl moieties, but not just any hydroxyl moieties—non-acidic hydroxyl moieties.

As noted above, Effing does not disclose or suggest such a patch. As further noted above, a fair reading of Effing, when taken as a whole, actually teaches against that which only Applicants have demonstrated to be of therapeutic value, i.e., adhesive patches suitable for the transdermal administration of granisetron, wherein the adhesive is an acrylic adhesive containing non-acidic hydroxyl moieties, with a physiologically effective amount of granisetron being loaded in the adhesive.

Further reliance on Sanger is unable to cure the deficiencies of Effing, since Sanger adds nothing to the consideration of what a transdermal patch for the delivery of granisetron should look like.

Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a), are respectfully requested.

## Conclusion

In view of the above remarks, reconsideration and favorable action on all claims are respectfully requested. In the event any matters remain to be resolved in view of this communication, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved.

Respectfully submitted,

Date August 28, 2008

By _____

Stephen E. Reiter
Attorney for Applicant
Registration No. 31,192

FOLEY & LARDNER LLP
Customer Number: 30542
Telephone: (858) 847-6711
Facsimile: (858) 792-6773